Assessment of diastolic chamber properties of the right ventricle by global fitting of pressure–volume data and conformational analysis of 3D + T echocardiographic sequences

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Purpose

Right ventricular (RV) dysfunction is a major prognosis determinant in many cardiovascular diseases. However, the physiological basis of RV diastolic function remains unclear [1]. Diastolic function is regulated by active and passive chamber properties. Active relaxation accounts for myofilament unbridging. Passive mechanical properties are derived from elastic chamber deformation when it is filled below or beyond its equilibrium volume (V_0; i.e. chamber volume at zero transmural pressure). Passive forces acting below V_0 account for elastic restoring forces, whereas those acting above V_0 are defined by ventricular stiffness. Currently, the analysis of pressure and volume (PV) data is indispensable for assessing diastolic chamber properties. Classical methods of PV data analysis focus on the characterization of relaxation and stiffness at specific times of diastole. Early diastole pressure–time exponential fitting characterizes relaxation whereas stiffness is estimated by fitting the curvilinear end-diastolic PV relationship from multiple beats during preload manipulation [2]. Recently, an algorithm based on global optimization has been validated to analyze left ventricular (LV) PV data providing most accurate indices of diastolic function by decoupling active and passive mechanical chamber properties [3]. The objectives of the present study were to characterize, for the first time in vivo, the relative contribution of RV active and passive diastolic chamber properties to RV filling and analyze their relationship with RV conformational changes during RV overload.

Methods

Thirteen minipigs were instrumented with a pressure-conductance catheter in RV. Acute preload reduction was induced with a balloon placed in the inferior vena cava (IVC). PV data were acquired during transient IVC occlusion during inotropic modulation, volume overload and during acute RV failure induced by infusion of *E. coli* lipopolysaccharide. 3D echocardiography was performed in each

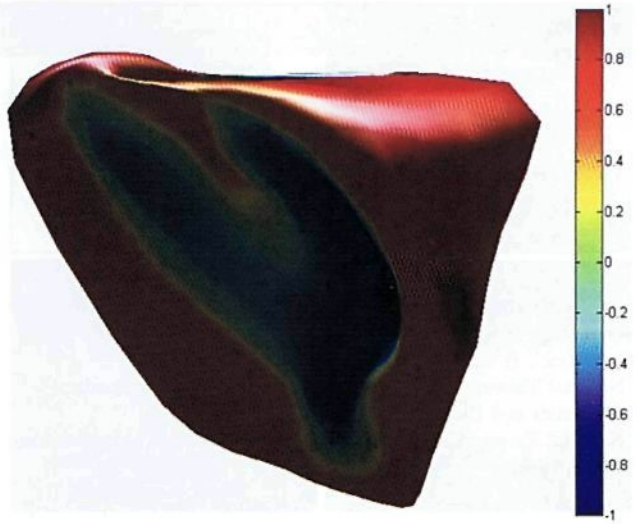

Fig. 1 Shape-index scale computing for a RV mesh at end diastole

phase. Indices of RV diastolic function were obtained with a numerical global optimization algorithm. Thus, diastolic pressure is defined as the resultant of adding active (P_a) and passive (P_p) forces acting throughout the full diastolic period. These pressure components are defined by relaxation constant (t), equilibrium volume (V_0), stiffness constants below and above V_0 (S_- and S_+) and volume asymptotes (V_m and V_d). 3D echocardiography RV images were analyzed off-line using commercial software and the inner surface meshes were further processed. After RV surface segmentation curvature parameters were calculated. Local minimum, maximum and mean curvatures, as well as shape-index (ratio of the maximum and minimum curvatures difference to the mean curvature) were computed for each triangle in the mesh (Fig. 1) [4]. Linear mixed-effects models (R, version 2.15.1) were used for data analysis, accounting for animal random effects.

Results

The interventions modulated RV hemodynamics as expected (see Table 1). The numerical algorithm converged in all data sets (n = 224). Passive restoring forces generated sub-atmospheric suction in all phases, significantly contributing to rapid filling. Remarkably, maintenance of suction despite severe acute RV overload was possible by shifting the passive PV relationship by increasing V_0 (see Table 1). This mechanism enhanced rapid filling by increasing the RA-RV pressure gradient and lowering RV diastolic pressures (Fig. 2) Conformational analysis demonstrated that both V_0 and the stiffness constant below V_0 (S_-) were significantly related to the degree of the RV septum bulging towards the LV at end-systole ($p < 0.05$). In turn, septal curvature was significantly related to the RV-LV transeptal pressure gradient ($p < 0.01$).

Conclusion

Diastolic suction caused by passive elastic restoring forces is a major determinant of RV filling. During acute overload, the curvature of the interventricular septum determines the magnitude of these restoring

Table 1 Effects of acute hemodynamic interventions on RV function and diastolic properties

	Baseline	Esmolol	Dobutamine	Volume	Endotoxin (30 min)	Endotoxin (180 min)
Heart Rate (bpm)	92 (85 to 100)	84 (77 to 92)*	118 (110 to 126)*	99 (91 to 107)	89 (81 to 97)	114 (106 to 122)*
Cardiac Output (l/min)	2.3 (2 to 2.6)	2 (1.7 to 2.3)*	2.7 (2.4 to 3)*	2.9 (2.6 to 3.3)*	2.2 (1.9 to 2.5)	2.4 (2 to 2.7)
Peak RVP (mm Hg)	29.8 (25.1 to 34.5)	28.4 (23.7 to 33.1)	36.4 (31.4 to 41.3)*	42.4 (37.3 to 47.6)*	41.9 (37.1 to 46.7)*	45.5 (40.7 to 50.3)*
EDP (mm Hg)	5.4 (4.4 to 6.5)	6.8 (5.8 to 7.8)*	4.1 (3 to 5.2)	14.9 (13.7 to 16)*	9 (8 to 10.1)*	6.9 (5.8 to 7.9)*
EDV (ml)	47 (40 to 54)	48 (41 to 55)	42 (35 to 49)*	56 (49 to 63)*	53 (46 to 60)*	61 (54 to 68)*
RVEF (%)	0.53 (0.49 to 0.58)	0.49 (0.45 to 0.54)	0.57 (0.52 to 0.62)	0.55 (0.51 to 0.6)	0.46 (0.42 to 0.51)*	0.36 (0.31 to 0.4)*
τ (ms)	41 (36 to 46)	39 (34 to 44)	29 (24 to 35)*	64 (59 to 70)*	40 (35 to 45)	46 (41 to 51)
V_0 *(ml)*	30 (24 to 37)	29 (23 to 35)	28 (21 to 34)	32 (25 to 38)	11 (25 to 38)	45 (39 to 52)*
dP/dV *at* V_0 *(mm Hg/ml)*	0.3 (0.2 to 0.3)	0.3 (0.3 to 0.4)	0.2 (0.2 to 0.3)	0.5 (0.5 to 0.6)*	0.3 (0.2 to 0.3)	0.3 (0.2 to 0.3)

Values show the estimated fixed effects (95% CI) from mixed models controlling for repeated measures within animal. *$p < 0.05$ vs. baseline. *RVP*, right ventricular pressure; *EDP*, RV end-diastolic pressure; *EDV*, RV end-diastolic volume; *RVEF*, right ventricular ejection fraction; τ, relaxation constant; V_0, equilibrium volume.

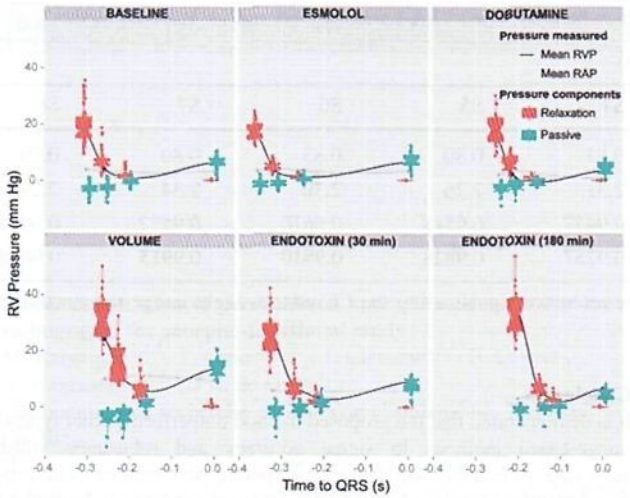

Fig. 2 Bar charts of active (in *red*) and passive (in *blue*) component of estimated pressure and mean measured pressure (*black line*) during diastole

forces. For the first time, these aspects of diastolic function can be analyzed in vivo by global optimization PV data analysis and shape conformational analysis of 3D + t echocardiographic sequences.

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